General

Guideline Title

Squamous cell carcinoma of the vulva.

Bibliographic Source(s)

Alberta Provincial Gynecologic Oncology Team. Squamous cell carcinoma of the vulva. Edmonton (Alberta): CancerControl Alberta; 2013 Sep. 10 p. (Clinical practice guideline; no. GYNE-006). [28 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Alberta Provincial Gynecologic Oncology Tumour Team. Squamous cell carcinoma of the vulva. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Aug. 9 p. (Clinical practice guideline; no. GYNE-006). [28 references]

Recommendations

Major Recommendations

Staging is based on the Fédération Internationale de Gynecologie et d'Obstétrique (FIGO) classification system, which was updated in 2010. A detailed description of this staging system can be found in the Appendix in the original guideline document.

Pre-operative Investigations

Investigations should include:

- History and clinical exam, biopsy
- Chest x-ray
- Blood work (complete blood count [CBC], liver function tests [LFT], renal function studies)

The following investigations could be considered, as clinically indicated:

- Computed tomography (CT) chest/abdomen/pelvis
- Examination under anesthesia (EUA) cystoscopy +/- sigmoidoscopy/proctoscopy, as clinically indicated

Primary Treatment

- Patients with a locally advanced primary or nodal disease should be referred for multidisciplinary clinical evaluation.
- An expert pathology review should be performed by a pathologist with experience in gynecologic pathology.

- Surgical management of the primary tumour and the lymph nodes depends on the size and location of the primary tumour (see the table below) (GOG 173 Study, unpublished results).
- Radical radiotherapy could be considered as an alternative to surgery in patients deemed unsuitable for surgery because of site or extent of disease, or where preservation of the clitoris or anal sphincter is desired.
- In patients with tumours >2 cm, chemoradiotherapy could also be considered as an alternative to surgery in patients deemed unsuitable for surgery because of site or extent of disease, or where preservation of the clitoris or anal sphincter is desired.

Table. Surgical Management of Squamous Cell Carcinoma of the Vulva

Tumour Size (cm)	Invasion (mm)	Location	Recommended Surgery
<2	<1	Lateral or central	Consider wide local excision
<2	<5	Lateral	Consider radical local excision with unilateral lymphadenectomy
<2	<5	Central*	Consider radical local excision with bilateral lymphadenectomy
<2	>5	Lateral	Consider radical vulvectomy with unilateral or bilateral lymphadenectomy
<2	>5	Central*	Consider radical vulvectomy with bilateral lymphadenectomy; separate groin incisions and unilateral lymphadenectomy for select early lesions may reduce morbidity
>2	Any	Lateral or central	Consider radical vulvectomy with bilateral lymphadenectomy; separate groin incisions and unilateral lymphadenectomy for select early lesions may reduce morbidity

*Up to 1 cm from midline

- Chemoradiotherapy is recommended, as primary definitive treatment in patients with extension to adjacent perineal structures and/or positive nodes.
    - Chemotherapy options include: fluorouracil (5-FU) alone, 5-FU plus cisplatin, or 5-FU plus mitomycin-C, or cisplatin alone, based on patient factors (i.e., renal insufficiency, ototoxicity, deafness).
    - Radiotherapy volume and dose will be individualized by the radiation oncologist.

Adjuvant Treatment

- Stage IA: the preferred treatment for stage IA disease is wide local excision (WLE) only.
- Stage IB: post-operative radiotherapy could be considered for close positive margins, at the discretion of the radiation oncologist.
- Stage II: post-operative radiotherapy could be considered for close positive margins, at the discretion of the radiation oncologist.
- Stage III:
    - Patients who are pathologically node positive should be referred to radiation oncology for clinical evaluation.
    - For patients with one lymph node metastasis (<5 mm and no extracapsular extension) post-operative radiotherapy is not recommended.
    - For patients with two or more lymph node metastases (≥5 mm) or three or more lymph node metastases (<5 mm), and for patients with positive nodes with extracapsular spread, post-operative radiotherapy is recommended.
    - If findings are positive for a unilateral groin node dissection for a small (<2 cm) lateral lesion, dissection of the contralateral groin is recommended.
    - Adjuvant local radiotherapy should also be considered for close margins.
- Stage IVA and IVB: for patients with invasion to regional (2/3 upper) structures or distant sites, with or without positive nodes, post-operative radiotherapy is recommended.
    - Adjuvant local radiotherapy should also be considered for close margins.

Follow-up and Surveillance

Patients treated with chemoradiotherapy as primary definitive treatment should be seen as follows:

- Clinical exam at 4 to 6 weeks
- Other tests as clinically indicated (i.e., suspicious clinical exam):

    - Imaging with CT or positron emission tomography (PET)-CT, as indicated
    - EUA with biopsy, post-treatment, if outpatient exam is not possible
- If imaging or biopsy is positive, consider salvage surgery

Long-term follow-up of all patients should include:

- Year 1: every 3 months, or as clinically indicated
- Year 2: every 4 months, or as clinically indicated
- Years 3–5: every six months, or as clinically indicated

Clinical Algorithm(s)

The following algorithms are provided on the Alberta Health Services Web site :

- Algorithm for the diagnosis & referral of squamous cell carcinoma of the vulva (GYNE-006)
- Algorithm for the management of early stage squamous cell carcinoma of the vulva (GYNE-006)
- Algorithm for the management of advanced stage squamous cell carcinoma of the vulva (GYNE-006)

Scope

Disease/Condition(s)

Squamous cell carcinoma of the vulva

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Obstetrics and Gynecology

Oncology

Pathology

Radiation Oncology

Surgery

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To recommend options for the management of vulvar cancer, based on the best evidence available

Target Population

Adults over the age of 18 years with squamous cell carcinoma of the vulva

Note: This guideline does not address patients with other vulvar cancer histologies, including adenocarcinoma, basal cell carcinoma, and melanoma.

Interventions and Practices Considered

Evaluation (Pre-operative Investigations)

1. History and clinical exam, biopsy
2. Chest x-ray
3. Blood work (complete blood count [CBC], liver function tests [LFT], renal function studies)
4. Computed tomography (CT) chest/abdomen/pelvis
5. Positron emission tomography (PET)-CT
6. Examination under anesthesia (EUA) cystoscopy +/- sigmoidoscopy/proctoscopy, as clinically indicated

Treatment/Management

1. Referral for multidisciplinary clinical evaluation
2. Expert pathology review
3. Surgical management based on tumour size, invasion, and location
    - Wide local excision (WLE)
    - Radical local excision with unilateral or bilateral lymphadenectomy
    - Radical vulvectomy with unilateral or bilateral lymphadenectomy
4. Radical radiotherapy as an alternative to surgery
5. Chemoradiotherapy
6. Chemotherapy (fluorouracil [5-FU] alone, 5-FU plus cisplatin, 5-FU plus mitomycin-C, or cisplatin alone)
7. Adjuvant treatment based on disease stage (e.g., post-operative radiotherapy, dissection of the contralateral groin)
8. Follow-up and surveillance

Major Outcomes Considered

- Cancer-related death rate
- Relative risk of disease progression
- Progression-free interval
- Overall and disease-free survival
- Local control
- Recurrence rate

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (Patient or Population, Intervention, Comparisons, Outcomes).

Guideline Questions

- What is the role of post-operative, adjuvant radiotherapy in early stage vulvar cancer?
- What is the role of definitive radiotherapy or chemoradiotherapy in advanced stage vulvar cancer?
- What is the role of sentinel lymph node biopsy in patients with clinically negative nodes, with tumours <2 cm?
- What is the role of surgery in patients with metastasis to the inguinofemoral nodes?
- What is the most appropriate follow-up schedule for advanced stage patients treated with chemoradiotherapy only?

Search Strategy

Entries to the Medline and EMBASE databases and clinical practice guideline databases (e.g., National Guideline Clearinghouse, CancerView, etc.) were searched for evidence relevant to this topic. Search terms included: neoplasm AND vulva or vulvar, with limits of studies in humans, clinical trials, and studies in English. Studies that did not report response rates or survival rates were further excluded.

The initial search in 2011 returned a total of 55 relevant studies, which included clinical trials, retrospective studies, and case studies. The search was repeated in 2013 and returned a total of three relevant citations.

Existing guidelines considered for this review include the following: Society of Obstetricians and Gynaecologists of Canada guidelines (2006), National Cancer Institute guidelines (2009), the Royal College of Obstetricians and Gynaecologists guidelines (2006), and the BC Cancer Agency (BCCA) guidelines (2000).

Number of Source Documents

The initial search in 2011 returned a total of 55 relevant studies, which included clinical trials, retrospective studies, and case studies. The search was repeated in 2013 and returned a total of 3 relevant citations.

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Gynecologic Oncology Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic will be assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulate the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

An effort was made to either adapt or adopt the most appropriate guidelines from other sources so that work wasn't duplicated. An evidence based perspective was used to draft proposals. Where evidence was weak, recommendations were based on group consensus.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Gynecologic Oncology Tumour Team.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it will be sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to

submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of squamous cell carcinoma of the vulva

Potential Harms

For advanced vulvar cancer, neoadjuvant radiation with or without chemotherapy followed by radical surgery should be considered the best option for management. However, this may be associated with more morbidity than either radiotherapy or chemotherapy alone with surgery.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Gynecologic Oncology Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report

Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Aug (revised 2013 Sep)

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

There was no direct industry involvement in the development or dissemination of this guideline.

Guideline Committee

Alberta Provincial Gynecologic Oncology Tumour Team

Composition of Group That Authored the Guideline

Members of the Alberta Provincial Gynecologic Oncology Tumour Team include gynecologic oncologists, radiation oncologists, medical oncologists, pathologists, nurses, and pharmacists.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Gynecologic Oncology Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Gynecologic Oncology Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

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Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 19, 2012. The information was verified by the guideline developer on February 1, 2013. This summary was updated by ECRI Institute on April 28, 2014. The updated information was verified by the guideline developer on June 6, 2014.

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